#### ABSTRACT

International infant mortality statistics have caused concern in the United States, since the US ranking relative to other developed countries has declined since World War II. This paper suggests that there may be international differences in reporting of very-low-birthweight infants and perinatal deaths and that such reporting differences bias comparisons of national perinatal and infant mortality rates. Efforts must be made to adopt standard conventions for the inclusion of small, early infants and fetal deaths in rate calculations. (Am J Public Health. 1994;84:850-852)

## International Infant Mortality Rates: Bias from Reporting Differences

Embry M. Howell, PhD, and Béatrice Blondel, PhD

#### Introduction

Because of their ready availability and recognized importance as health and social indicators, infant mortality rates are routinely used for comparing countries. These statistics have become a source of concern in the United States, because it appears that the degree of decline in US rates has been lower than in other developed countries since World War II.<sup>1</sup>

The usefulness of crude infant mortality rates in international comparisons is questionable because of differences in the registration of births and deaths among very-low-birthweight (<1500 g) infants. In most European Community countries, registration is limited to births and fetal deaths above 27 weeks of gestation.<sup>2</sup> In Norway, registration is at 16 weeks and above,3 and, in other places such as Osaka Province, Japan, and parts of the United States, all products of conception may be registered even though such registration is certainly incomplete for early fetal deaths. Common practices may also vary at local levels.4-7 These differences in laws and customs regarding registering fetal deaths and live births have an impact on reported mortality rates.8,9

#### Methods

The purpose of this paper is to present data on birthweight distributions for births and fetal deaths from a wide range of countries and to show how registration and reporting bias may affect mortality rates. We used national samples of births in the United States (1980) and France (1981); Michigan state vital statistics (1984); a birth registry from Lorraine, France (1984); and vital statistics from several countries or regions that were included in the International Collaborative Effort on Infant Mortality sponsored by the US National Center for Health Statistics.<sup>10</sup> The International Collaborative Effort countries and regions were England and Wales; Hungary; Osaka Province, Japan; Norway; Sweden; and several states in the United States: California, Georgia, Michigan, Minnesota, Missouri, North Carolina, Utah, and Wisconsin. To analyze underreporting of very small infants and the possible misclassification of fetal deaths, we also developed hypothetical data to illustrate how reporting may bias international comparisons of infant mortality rates.

#### Results

Table 1 provides sample survey data, vital statistics, and birth registry data from France and the United States. While French infants were smaller, on average, there were fewer reported very-low-birthweight births proportionately in France. Because mortality rates are extremely high in the very-low-birthweight category (more than 400 per 1000), any underreporting in this category will bias mortality rates. Table 1 also shows that, among fetal and neonatal deaths, the proportion of fetal deaths was substantially higher in Lorraine than in Michigan.

Other data show that in 1985 the United States, Norway, and Osaka Province, Japan, reported between 0.2% and 0.4% of births and fetal deaths as less than 500 g (top panel of Table 2). The proportion of very-low-birthweight infants and fetal deaths ranged from 0.7% in Sweden to 1.5% in Osaka, Japan. Many of these differences are due to differences in reporting requirements for fetal deaths. After excluding all fetal deaths under 28 weeks' gestation (bottom panel of Table 2), we found similar very-low-birthweight rates in Osaka, Norway, and Sweden, while the rates shown before exclusions are quite different.

The proportion of perinatal deaths reported as fetal deaths ranged from 33% in Hungary to 68% in France (Table 3), suggesting large differences across countries in categorizing live births and fetal deaths. These classification differences could bias international infant mortality rate comparisons, since fetal deaths are

Embry M. Howell is with Mathematica Policy Research, Washington, DC. Béatrice Blondel is with the Epidemiology Research Unit on Women and Children's Health, INSERM, Villejuif, Cedex, France.

Requests for reprints should be sent to Embry M. Howell, PhD, Mathematica Policy Research, 600 Maryland Ave, SW, Suite 550, Washington, DC 20024.

This paper was accepted August 3, 1993.

TABLE 1—Low-Birthweight Rates, Mean Birthweight, and Perinatal Mortality
Rates: United States and France

	Natality Sur	veysª	Regional Datab		
	United States, 1980	France, 1981	Michigan, 1984	Lorraine, 1984	
Mean birthweight, g	3365	3322	3274	3250	
Very low birthweight, % < 1500 g	0.8	0.3	1.3	1.0	
Moderately low birthweight, %1500–2499 g	5.0	4.8	5.6	5.5	
Perinatal mortality rate, <sup>c</sup> deliveries <1500 g	• • •		428.9	470.1	
Perinatal mortality rate, <sup>c</sup> deliveries 1500–2499 g	• • •		51.2	59.2	
Perinatal deaths that were fetal deaths, %		• • •	43	61	

Source. Raw data were obtained from data tapes of the US Natality Survey, 1980; French Natality Survey, 1981; Michigan Vital Statistics; and Lorraine Birth Registry.

TABLE 2—Very-Low-Birthweight Rates (%) for Selected Countries, 1985

Birthweight, g	England and Wales	Hungary	Japan (Osaka, 1984)	Norway	Sweden	United States
All report	ed live births	and fetal d	eaths, regardle	ss of gest	ational ag	je
< 500	0.0	0.0	0.4	0.3	0.0	0.2
500-999	0.3	0.6	0.6	0.4	0.2	0.6
1000-1499	0.7	1.1	0.4	0.5	0.5	0.7
Total < 1500	1.0	1.7	1.5	1.2	0.7	1.5
All reporte	ed live births a	nd fetal de	eaths of 28 wee	ks' gestat	ion or mo	re
< 500	0.0	0.0	0.0	0.0	0.0	0.2
500-999	0.3	0.5	0.2	0.2	0.2	0.5
1000-1499	0.7	1.1	0.4	0.5	0.5	0.6
Total < 1500	1.0	1.7	0.6	0.7	0.7	1.3

Source. Data are from International Collaborative Effort on Perinatal and Infant Mortality. 10

not included in routinely reported infant mortality rates.

Hypothetical data show how underreporting could bias perinatal mortality rates. In a hypothetical country, the actual very-low-birthweight proportion is 1.0%, but the reported percentage is only 0.5. Assume a very-low-birthweight perinatal mortality rate of 470 per 1000 and 100 000 reported live births and fetal deaths. There are actually 470 very-low-birthweight perinatal deaths, but only 235 are reported. The reported perinatal mortality rate is 15 per 1000, but correcting for underreported deaths would raise this rate substantially to 17.3 per 1000.

Another hypothetical example illustrates the impact of differences in the classification of fetal deaths. Two hypothetical countries each have 55 000 live births and fetal deaths, 1000 perinatal deaths, and identical perinatal mortality rates of 18.2 per 1000. However, in the first country 40% of perinatal deaths are classified as fetal deaths, while the proportion is 60% in the second country. Assuming identical postperinatal mortality, the infant mortality rates are very different in the two countries: 14.0 per 1000 in the first country and only 10.4 per 1000 in the second country. This is entirely due to differences in the propor-

TABLE 3—Proportion of Fetal
Deaths among Perinatal
Deaths: Selected
Countries, 1985

Country	Fetal Deaths, %		
England and Wales	56		
France	68		
Hungary	33		
Japan	67		
Norway	58		
Sweden	54		
United States	43		

Note. Fetal deaths of 28 weeks' gestation or more and infant deaths in the first 7 days of life are included.

tion of fetal deaths among perinatal deaths.

#### Discussion

Differences in the completeness of reporting of low-birthweight births or fetal deaths and the classification of fetal deaths may substantially bias international comparisons. Such bias was suggested by Lee et al.<sup>11</sup> when they found that the poor ranking of the United States was mainly explained by a high rate of very-low-birthweight babies.

Numerous researchers have stressed the effects of variations in registration limits and the importance of standard rules for international comparisons. 12,13 The World Health Organization recommends that national statistics include all fetuses and infants weighing at least 500 g. In all countries, such recommendations should be used and guidelines developed for health care professionals emphasizing the importance of complete and accurate reporting of vital events. Until reporting becomes more uniform across countries, it is desirable to exclude the smallest birthweight births and to combine infant and fetal deaths before making international comparisons.

#### Acknowledgments

This work was funded, in part, by grant HS06621 from the Agency for Health Care Policy and Research, Rockville, Md.

This paper was presented at the 119th Annual Meeting of the American Public Health Association, October 1991, Atlanta, Ga.

Francis Notzon, PhD, of the US National Center for Health Statistics provided access to data on birthweight and infant and fetal

<sup>&</sup>lt;sup>a</sup>Singleton live births and fetal deaths of 28 weeks' gestation or more.

bAll live births and fetal deaths of 500 g or more.

Infant deaths in the first 28 days of life plus fetal deaths divided by total births and fetal deaths, multiplied by 1000.

Source. Data are from the International Collaborative Effort on Perinatal and Infant Mortality.<sup>10</sup>

mortality for selected countries and helpful comments on this paper. Paul Vert, MD, provided access to data for Lorraine, France.

#### References

- Health United States 1991. Hyattsville, Md: US Dept of Health and Human Services; 1992.
- Kaminski M, Bouvier-Colle MH, Blondel B. La mortalité des jeunes dans les pays de la communauté européénne. Paris, France: Doin: 1985.
- Births in the Nordic Countries: Registration of the Outcome of Pregnancy: 1978–1983.
   Reykjavik, Iceland: Nordisk Medicinal-Statistisk Kommitté; 1987.
- 4. Doornbos JPR, Nordbeck HJ, Treffers PE. The reliability of perinatal statistics in the

- Netherlands. Am J Obstet Gynecol. 1987; 156:1183–1187.
- Keirse MJNC. Perinatal mortality rates do not contain what they purport to contain. *Lancet.* 1984;1:1166–1169.
- 6. Dunn PM, Lashford AM. Limit of fetal viability. *Lancet*. 1984;1:1079–1080.
- Fenton AC, Field DJ, Mason E, Clarke M. Attitudes to viability of preterm infants and their effect on figures for perinatal mortality. BMJ. 1990;300:434–436.
- Blondel B, Grandjéan BH, Kaminski M, et al. Criteria for registering births. *Lancet*. 1991:337:981.
- Scott MJ, Ritchie JWK, McClure BG, McReid M, Halliday HL. Perinatal death recording: time for a change? BMJ. 1987; 282:707-710.

- Proceedings of the International Collaborative Effort on Perinatal and Infant Mortality. Hyattsville, Md: US Dept of Health and Human Services; 1992; 3.
- Lee K-S, Paneth N, Gartner LM, Pearlman M. The very low-birthweight rate: principal predictor of neonatal mortality in industrialized populations. *J Pediatr.* 1980;87:758– 764.
- Kline J, Stein Z, Susser M. Conception to Birth. Epidemiology of Prenatal Development. New York, NY: Oxford University Press; 1989.
- 13. Working Group on the Very Low Birthweight Infant. European community collaborative study of outcome of pregnancy between 22 and 28 weeks gestation. *Lancet*. 1990;336:782–784.

### ABSTRACT

People handling anticancer drugs or their wastes may absorb these potent genotoxic agents. The aim of this study was to determine the utility of some general urinary markers among 24 female oncology nurses handling these drugs in comparison with 25 "unexposed" nurses. The markers were the Salmonella typhimurium reverse and forward mutation assays, total thioethers, and D-glucaric acid. The reverse mutation assay was the most specific and sensitive marker for anti-cancer drug exposure. Use of the marker battery was no great advantage as a screening tool relative to use of the reverse mutation assay alone. Better recording of work practices in nurse work logs would have improved interpretation of results. (Am J Public Health. 1994;84:852-855)

# Urinary Biological Monitoring Markers of Anticancer Drug Exposure in Oncology Nurses

Mary Anne Newman, PhD, MS, Barbara G. Valanis, DrPH, Rita S. Schoeny, PhD, and Shane Que Hee, PhD

#### Introduction

Anticancer drugs target cancers because cell division is rapid.1-3 These drugs affect other proliferating noncancerous tissues (bone marrow, hair follicles, gastrointestinal-nasopharyngeal and genitourinary tract epithelia, and developing embryos).1-5 Many antineoplastic drugs are carcinogens and teratogens.4 Adverse effects include irregular menstrual period. testicular function suppression, hair loss, chromosomal abnormalities, decreased white blood cells, liver damage, and spontaneous abortion, as well as light headedness, dizziness, nausea, headache, cough, and skin/mucous membrane and allergic reactions. 1-5 Settings where many of these drugs are administered or prepared (hospitals, home health agencies, pharmacies, waste handlers, and outpatient settings) need sensitive, selective, noninvasive, and inexpensive screening tests reflecting absorption of many anticancer drugs.

Four noninvasive, general urinary antineoplastic drug markers were assessed relative to oncology nurse work practices as part of ongoing research programs. <sup>6-14</sup> The markers were Salmonella typhimurium reverse and forward mutagenicity, total thioethers, and

D-glucaric acid. All increased for patients receiving high treatment doses.<sup>11</sup> The reverse mutation assay is the "gold standard" for detecting urinary point and frameshift mutagens.<sup>15</sup> About 60% of oncology nurse investigations<sup>1–4,7–10,15–26</sup> are positive. The forward mutation assay detects DNA large base deletions and insertions, base-pair changes, and frameshifts.<sup>27</sup> Thioethers reflect the glutathione detoxification of electrophiles, putative mutagens.<sup>15,28</sup> D-glucaric acid reflects microsomal mixed function oxidation in the liver and kidney and bladder β-glucuronidase activity.<sup>15,29</sup>

Mary Anne Newman is with Health Environments, Inc, Cincinnati, Ohio. Barbara G. Valanis is with the Kaiser-Permanente Center for Health Research, Portland, Ore. Rita S. Schoeny is with the ECAO Division, United States Environmental Protection Agency, Cincinnati, Ohio. Shane Que Hee is with the Department of Environmental Health Sciences, UCLA Center for Occupational and Environmental Health, UCLA School of Public Health, Los Angeles, Calif.

Requests for reprints should be sent to Shane Que Hee, PhD, Department of Environmental Health Sciences, UCLA School of Public Health, 10833 Le Conte Ave, Los Angeles, CA 90024-1772.

This paper was accepted September 30, 1993.